IQ and blood lead from 2 to 7 years:

Are the effects in older children the residual of high blood leads in 2 year olds?

Aimin Chen and Walter Rogan

Department of Health and Human Services
National Institutes of Health
National Institute of Environmental Health Sciences

Blood lead concentration

- **In US children, blood lead tends to peak at about 2 years, and then decline.**
  - Prenatal exposure
  - Postnatal exposure: leaded paint (most houses built before 1980 contain some leaded paint), dust
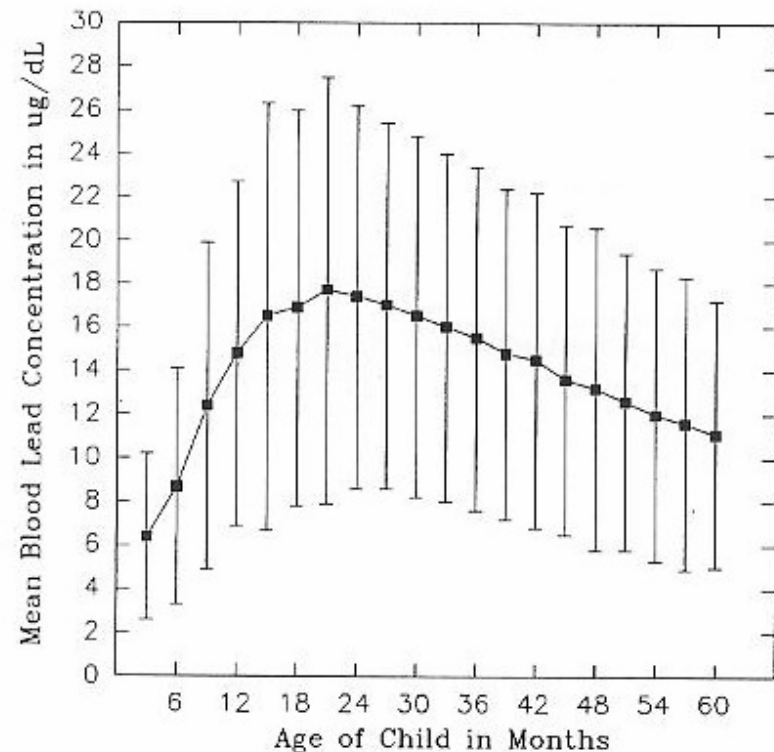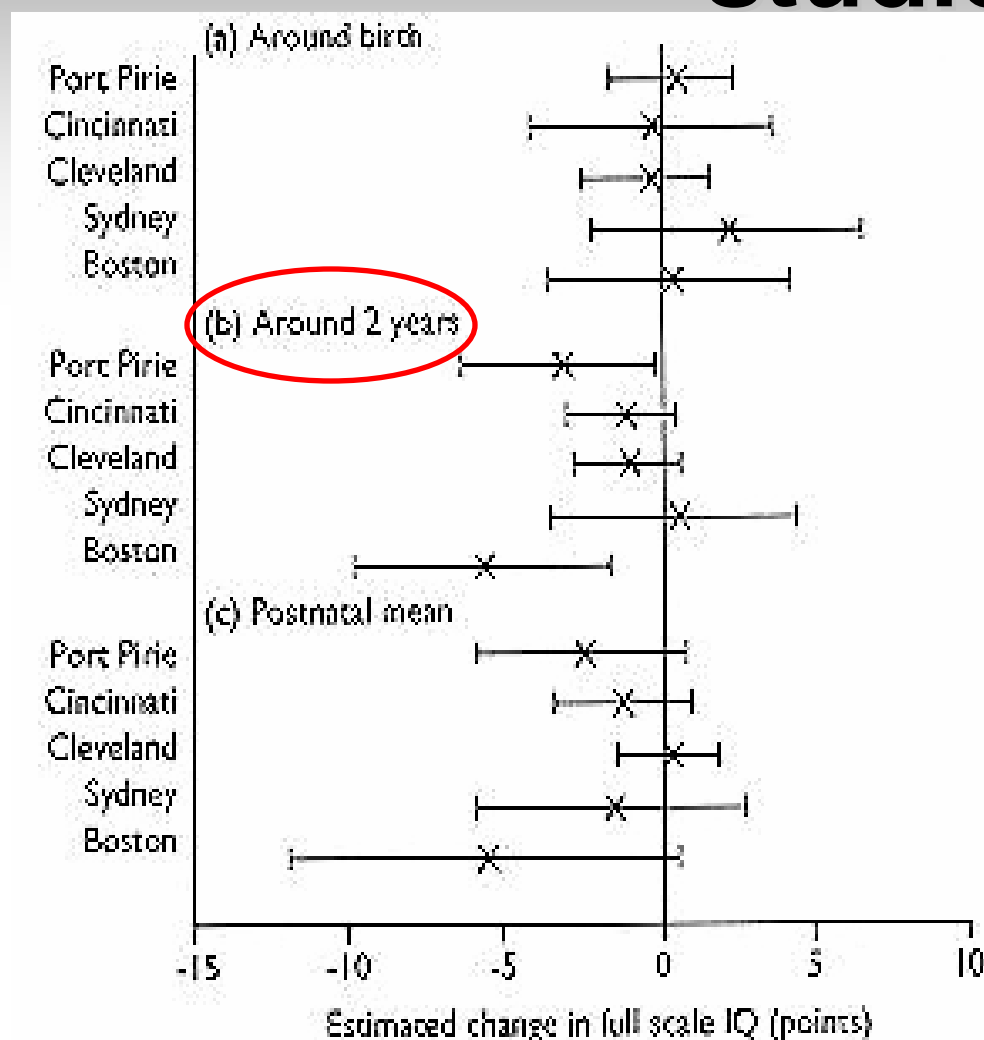

FIG. 1. Arithmetic mean (±SD) PbB concentrations from 3 to 60 months of age.

Dietrich et al. Neurotoxicol Teratol 1993

Meta-analysis of prospective studies

Meta-analysis results:

(a) 0.2 (-1.0, 1.4)

(b) -1.9 (-2.8, -0.9)

(c) -0.9 (-2.0, 0.3)

Prospective studies: estimated change in full scale IQ (and 95% CI) for increase in blood lead from 10 to 20 µg/dl

Pocock et al. BMJ 1994

Implication of peak lead effect

- To study threshold, need to recruit 2 year olds and follow them

- Screening of lead poisoning focusing on 1 and 2 year olds

- Clinical trials treating 2 year olds

Previous prospective studies

- In Boston, 57 mo and 10 y blood lead not associated with 10 y IQ

- In Cincinnati, mean blood lead during the 5th and 6th year associated with IQ at 6.5 years, but mean blood lead during the 2nd or 3rd year was not.

- In Rochester, concurrent blood lead and 5y IQ association slightly stronger than peak blood lead and 5y IQ association

- No study examined the question in detail

Study questions

- What is the strength of the association between blood lead and IQ at various time points?

- Do the cross-sectional associations seen in school age children represent residual effects from peak blood lead?

# Treatment of Lead-exposed Children (TLC) study

- Randomized placebo-controlled clinical trial of succimer, an oral chelator
- 1° outcome – IQ
- 780 children aged 12-33 months with blood lead concentration 20-44 µg/dL
- Follow-up to 60 months after treatment (age 7)
- Multi-center: Baltimore, Newark, Philadelphia, and Cincinnati

Lead and IQ measurements

- **Blood lead level (PbB)**
  - randomization (baseline); day 7, 28, 42 of each course of treatment; every 3-4 months in the follow-up
- **IQ**
  - Mental Development Index (MDI) from Bayley Scale of Infant Development-II (BSID-II) at baseline
  - Full scale IQ from Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) at 36 month follow-up
  - Full scale IQ from Wechsler Intelligence Scale for Children-III (WISC-III) at 60 month follow-up

  - Caregivers' IQ (88% mother) from Wechsler Adult Intelligence Scale-Revised (WAIS-R)
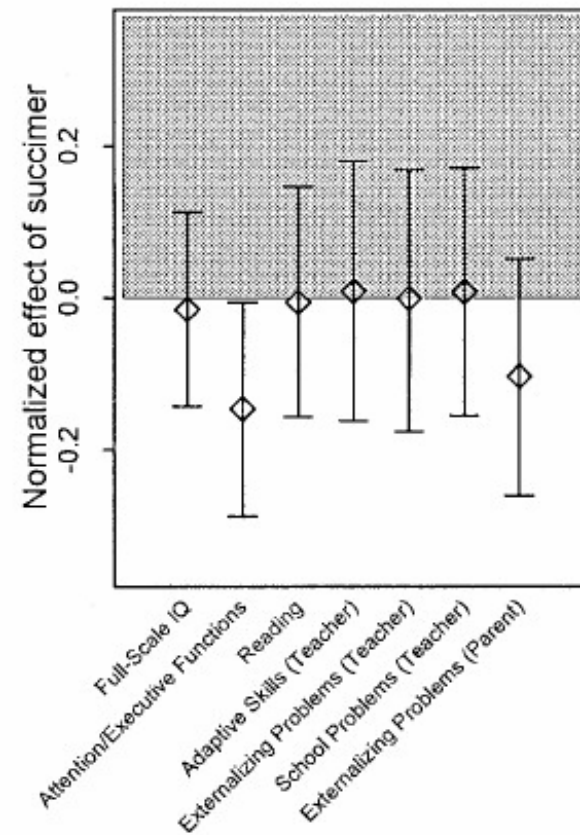
Blood lead level in TLC study
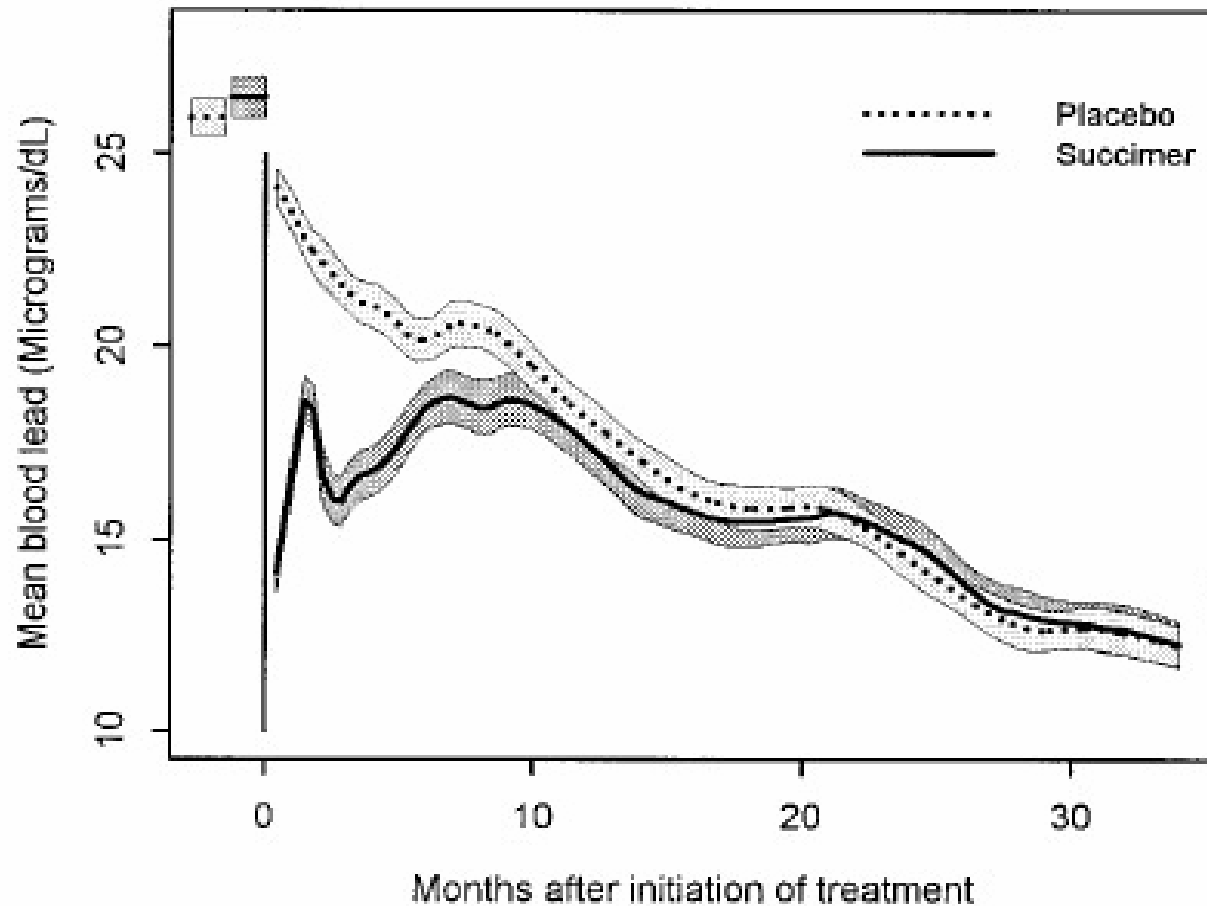
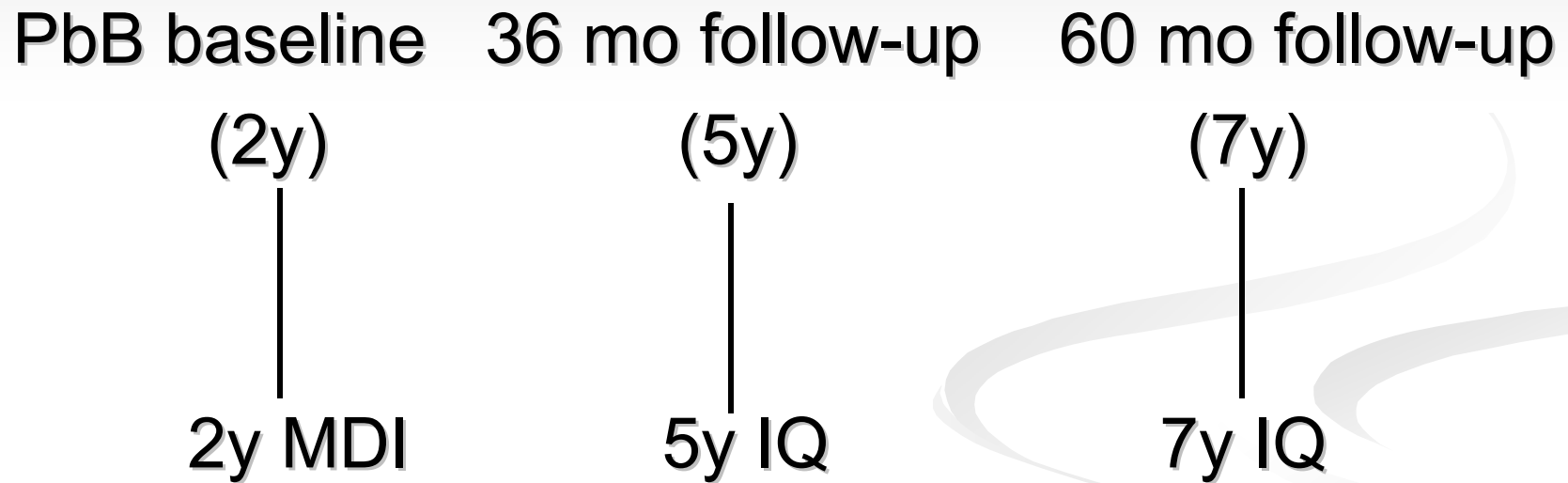# No IQ difference from treatment

WPPSI-R
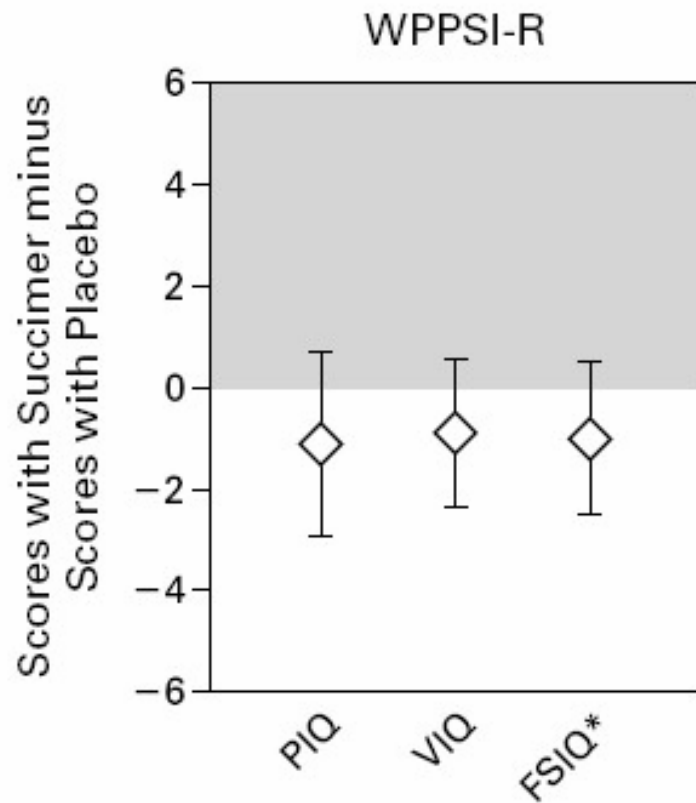
36 mo follow-up

60 mo follow-up

Statistical analysis

- General linear models

- Untransformed blood lead

- Covariates: Clinical center, race/ethnicity, sex, language, parent's education, parent's employment, single parent, age at blood lead test, caregiver's IQ

- No treatment effect on IQ, so succimer and placebo groups combined

Step 1

PbB baseline   36 mo follow-up   60 mo follow-up

(2y)   (5y)   (7y)

2y MDI   5y IQ   7y IQ

Step 1

PbB baseline   36 mo follow-up   60 mo follow-up
(2y)   (5y)   (7y)

2y MDI   5y IQ   7y IQ
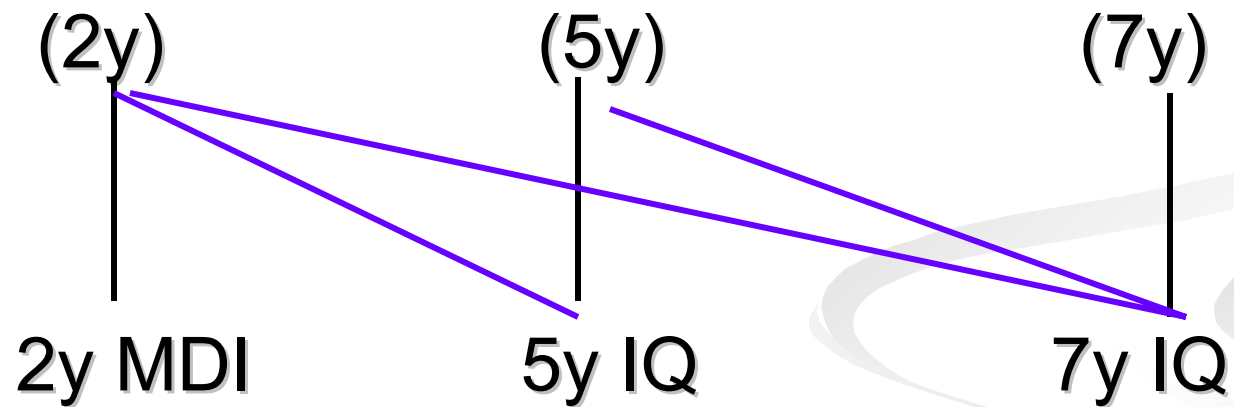
Step 2

- Both prior and concurrent PbB in the model

  - 5yIQ = 2yPbB + 5yPbB + Covariates

  - 7yIQ = 2yPbB + 7yPbB + Covariates

  - 7yIQ = 5yPbB + 7yPbB + Covariates

Results

- 396 children in succimer group, 384 in placebo group (total 780)
- Overall: African American 77%

    Male 56%

    Speaking English 95%

     Parent <high school education 40%

    Single parent 72%

    On public assistance 97%

IQ by PbB modeled separately

Outcome	β (95% CI) per 10 µg/dL PbB		
	2y	5y	7y
2y MDI	-2.9 (-4.7, -1.0)		
5y IQ	-2.3 (-4.1, -0.5)	-3.5 (-5.3, -1.7)	
7y IQ	-1.1 (-2.9, 0.7)	-2.9 (-4.8, -1.1)	-5.4 (-7.8, -2.9)

All adjusted for center, race, sex, language, parent's education, employment, single parent, caregiver's IQ and age at PbB test

Both prior and concurrent PbB in the model

Outcome	β (95%CI) per 10 µg/dL PbB		
	2y PbB	5y PbB	7y PbB
5y IQ	-1.2 (-3.1, 0.7)	-2.9 (-4.9, -0.9)	
7y IQ	0.1 (-1.8, 2.0)		-5.0 (-7.6, -2.4)
7y IQ		-1.2 (-4.1, 1.7)	-3.9 (-7.4, 0.0)

All adjusted for center, race, sex, language, parent's education, employment, single parent, caregiver's IQ and age at both PbB tests

Step 3

- Categorize prior and concurrent PbB into one variable (by corresponding medians)
- To reduce but may not eliminate possible collinearity.

Category	2y PbB (µg/dL)	5y PbB (µg/dL)
1 (ref)	$<Median_{2y}$	$<Median_{5y}$
2	$<Median_{2y}$	$\geq Median_{5y}$
3	$\geq Median_{2y}$	$<Median_{5y}$
4	$\geq Median_{2y}$	$\geq Median_{5y}$

2y and 5y PbB on 5y IQ

PbB (µg/dL)		n	5y IQ Mean	5y IQ Comparison
2y	5y			
<24.9	<11.4	227	84	referent
<24.9	≥11.4	137	79	-2.9 (-5.8, 0.1)
≥24.9	<11.4	138	82	0.4 (-2.5, 3.3)
≥24.9	≥11.4	228	78	-4.0 (-6.6, -1.5)

All adjusted for center, race, sex, language, parent's education, employment, single parent, caregiver's IQ and age at both PbB tests

2y and 7y PbB on 7y IQ

PbB (µg/dL)		n	7y IQ Mean	7y IQ Comparison
2y	7y			
<24.9	<7.2	187	89	referent
<24.9	≥7.2	114	85	-3.6 (-6.4, -0.7)
≥24.9	<7.2	121	89	-0.0 (-2.8, 2.7)
≥24.9	≥7.2	195	84	-3.7 (-6.2, -1.3)

All adjusted for center, race, sex, language, parent's education, employment, single parent, caregiver's IQ and age at both PbB tests

5y and 7y PbB on 7y IQ

PbB (µg/dL)		n	7y IQ Mean	7y IQ Comparison
5y	7y			
<11.4	<7.2	244	89	referent
<11.4	≥7.2	52	86	-2.3 (-5.9, 1.3)
≥11.4	<7.2	62	88	0.3 (-3.1, 3.7)
≥11.4	≥7.2	255	84	-3.8 (-6.0, -1.6)

All adjusted for center, race, sex, language, parent's education, employment, single parent, caregiver's IQ and age at both PbB tests

Strengths and limitations

- Large sample size, degree of testing, quality control, longitudinal, high retention rate

- Restricted population, no Home Observation for Measurement of the Environment (HOME) score

Conclusions

- We found a stronger relationship between PbB at 7y and IQ at 7y than between IQ at 7y and the higher 2y PbB

- The strength of the cross-sectional association increases over time

- Results support the idea that lead exposure continue to be toxic to children as they reach school age, not all the damage was done by the time children were 2-3 year old

Implication

- Lead exposure at about school age may affect cognition, and it is better to always keep PbB low

- The difficulties in preventing lead exposure ↑, but the potential for prevention ↑

Future work

- To examine the strength of the prospective and cross-sectional associations of lead and IQ using other cohorts
  - Individual cohort
  - Pooled or meta-analysis of several cohorts

Future work

- To study the prevention strategy that keeps blood lead low till school age and IQ improvement
  - Specific population in US with high lead exposure
  - Children in developing countries

Acknowledgments